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Short Review on Thiazole Derivative

Abida Qureshi*, Alka Pradhan

Department of Chemistry, Sarojini Naidu Govt Girls' Post Graduate College, Main Rd 2, No 6 Locality, Shivaji Nagar, Bhopal, MP 462016

ABSTRACT

Thiazole is aromatic, heterocyclic organic compound that have five membered molecular ring structures C_3H_3NS. Thiazole was first described by Hantzch and Weber in 1887. Prop confirmed its structure in 1889. The numbering of thiazole starts from sulphur atom. Numerous reports have appeared in the literature which highlights their chemistry and pharmacological uses. There is larger Pi-electron delocalization in thiazoles as compared to corresponding oxazoles and hence have greater aromaticity which is evidenced by the chemical shift of the ring protons in proton NMR spectroscopy indicating strong diamagnetic current. Mostly researches have maintained their interest in nitrogen and sulphur containing heterocyclic compounds through decades of historical development of organic. This paper aims to review the antimicrobial activities of thiazole during the past decades.

Keywords: Thiazole, Heterocyclic compounds, Oxazoles Biological activities,

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***Address for Correspondence:**

Abida Qureshi, Department of Chemistry, Sarojini Naidu Govt Girls' Post Graduate College, Main Rd 2, No 6 Locality, Shivaji Nagar, Bhopal, MP 462016

INTRODUCTION

Small ring heterocycles containing nitrogen and sulfur have been under investigation for a long time because of their important medicinal properties. Among the wide range of heterocycles explored to develop pharmaceutically important molecules, thiazoles have played an important role in medicinal chemistry. Thiazoles are one of the most intensively investigated aromatic five-membered heterocycles. Hanstzch and Weber in 1887 reported the first synthesis of thiazoles. Thiazole is involved in many natural products of biological importance. For example, the thiazolium ring present in vitamin B_1 serves as an electron sink, and its coenzyme form is important for the decarboxylation of alpha keto acids. Thiazole and its derivatives are very useful compounds in various fields of chemistry including medicine and agriculture. Also, thiazoles are synthetic intermediates and common substructures in a number of biologically active compounds such as various derivatives of penicillins.

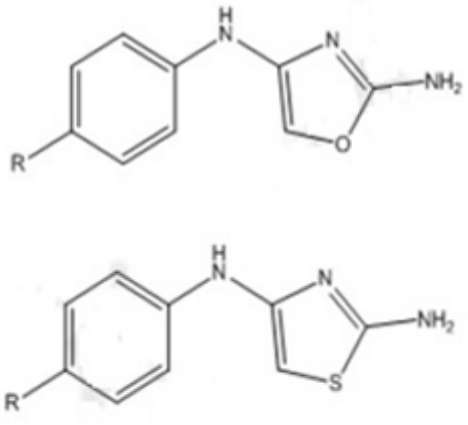
A survey of literature has shown that compounds having thiazole nucleus possess a broad range of biological activities such as anti-inflammatory[1], antibacterial[2], antifungal[3]. Although a variety of thiazole derivatives have been synthesized over years, the nucleus still possesses considerable characteristics to attract the chemists for designing of newer biologically active molecules.

On the basis of literature surveys thiazole derivatives have potential against antimicrobial activities as shown:

ANTIMICROBIAL ACTIVITIES

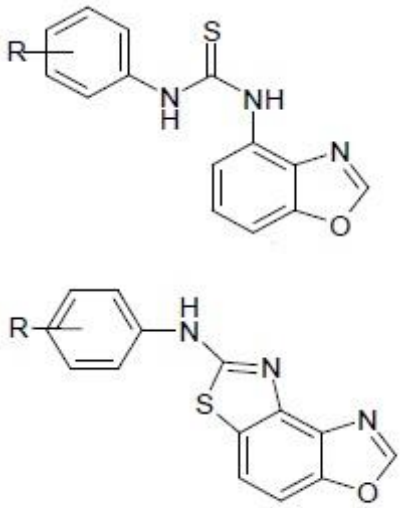
1. Sharshira[5] worked on a series of thiazoles prepared by incorporation of pyrazoline ring at position 2 of 2-hydrazinyl-N-(4-phenylthiazol-2-yl) acetamide by treating with chalcones. The structures of the newly synthesized compounds were determined on the basis of their elemental analyses and spectroscopic data such as IR and 1HNMR spectra. The antimicrobial activity of isolated heterocyclic compounds was evaluated against Gram-positive, Gram-negative bacteria and fungi. Most of the compounds showed a moderate degree of potent antimicrobial activity.

2. Some new antimicrobial agents synthesized by Mohanty[6], They carried out the reaction of anilines with chloroacetyl chloride to produce an intermediate, which undergoes condensation with urea and thiourea under microwave irradiation in the presence of ethanol to produce oxazole and thiazole derivatives. The synthesized compounds were characterized by spectral data such as IR, NMR and Mass. Compounds were screened for antimicrobial activity against strains of gram positive, and gram negative. All compounds showed moderate antibacterial activity.



[1]

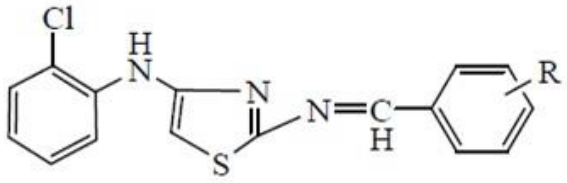
Vodela[7] synthesized series of various novel phenyl-(6H-thiazolo[4,5-e]benzoxazole-2-yl)-amines as have been synthesized by involving 4-nitro-1H-benzooxazole as starting material and 4-amino-1Hbenzooxazole, (1H-benzooxazole-4-yl)-dithiocarbamic acid methyl ester and 1-(1Hbenzooxazole- 4-yl)-3-phenyl-thioureas as intermediates. After structural confirmation, the title compounds were screened for their antimicrobial activity.



[2]

Work has also been done by Bhatt[8] on novel antimicrobial and antifungal agents. In the study Benzil (α-Diketone) when reacted with guanidene in presence of ethanolic alkali, condensation followed by pinacole-pinacoline rearrangement result in the formation of compound 2-imino-5,5-diphenylimidazolidin-4-one. Cyclisation of this compound with chloroaceticacid to give 6,6-diphenyl-1H-imidazo[1,2-a]imidazole-3,5(2H,6H)-dion a fused bicyclic compound. Condensation of methylene entity in imidazolidinone part with various aryl aldehyde yielded arylidene cyclic chalcones 2-benzylidene-6,6-diphenyle-1H-imidazo[1,2-a]imidazole3,5(2H,6H)-dione. The structures of the synthesized compounds were assigned on the basis of elemental analyses, IR and 1H NMR spectral data. The antibacterial and antifungal activities of the resulting derivatives were screened.

Schiff bases of 2-amino-4-(o-chloro anilino)-1, 3-thiazole were synthesized and screened for their antibacterial and antifungal activities by Karki[9]. The structures of these compounds were ascertained by UV, IR, 1H NMR, mass spectra and elemental analysis. The antibacterial activity of the synthesized schiff bases were evaluated against Gram positive bacteria such as *Staphylococcus aureus*, *Bacillus subtilis* and Gram negative bacteria like *Escherichia coli* and *Klebsiella pneumonia*. All the compounds had shown moderate to significant antibacterial activity amongst them. The antifungal activity was screened against two strains of fungi such as *Candida albicans* and *Aspergillus Niger*.



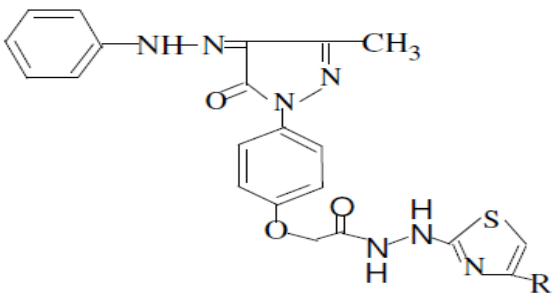
[3]

Patel[10] synthesized and characterized various spiro thiazolinone heterocyclic compounds. 4-(4-(6,7-dihydrothieno[3,2-c] pyridin- 5(4H)-ylsulfonyl)phenyl)-1-thia-4-azaspiro[4.5]decan-3-one. All the synthesized compounds were screened for their antimicrobial activity and it was observed that as the fusion of heterocyclic rings increases its shown higher antimicrobial activities.

Siddiqui[11] reviewed the five membered heterocyclic rings in their structure have an extensive spectrum of biological activities.

Salman[12] worked on reaction of imidazole-2-thione derivative with 2-chloro-N-p-tolylacetamide afforded the corresponding 2-(1H-imidazol-2-ylthio)-N-p-tolylacetamide. Reaction compound with different reagents such as p-chlorobenzaldehyde and p-chlorophenyl diazonium chloride afforded the corresponding arylidene derivative and hydrazone derivative. Reactions with carbon disulfide in dimethylformamide (DMF) in one equivalent potassium hydroxide afforded intermediate potassium sulphide salt, which on treatment with dilute hydrochloric acid and phenacyl bromide afforded the corresponding 2-[p-tolylcarbamoyl] ethanedithioic acid and 3-[benzo-ylmethylthio]- N-p-tolyl-3-thioxo-propaneamide. The structure of the newly synthesized compounds has been confirmed by elemental analysis and spectra data.

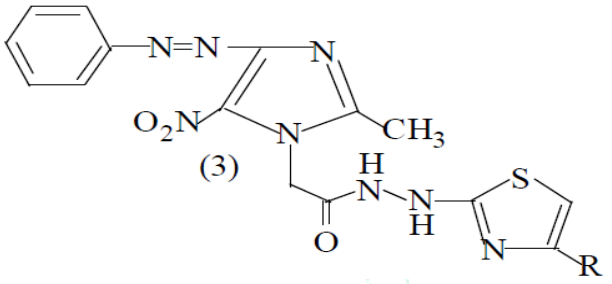
Naik[13] studied phenyl hydrazones and the compounds under study exhibited promising antimicrobial activity against all the tested microbes. The antimicrobial activity of title compounds were compared with that of standadards. The title compounds with p-nitrophenyl, p-chlorophenyl, p-bromophenyl were more active against bacteria, where as the compounds with substituents namely phenyl, p-toluyl, p-anisyl, p-hydroxyphenyl, p-nitrophenyl were more active against fungi than the other compounds under investigation.



[4]

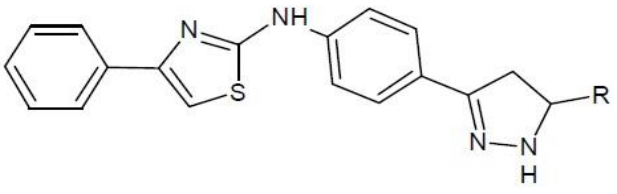
Hussein[14] worked on antimicrobial activity of some thiazole and thiazolo[3,2-a]pyridine derivatives. The data revealed that most of the synthesized compounds had varying degrees of inhibition against both bacteria and fungi. New thiazole and thiazolo[3,2-a]pyridine derivatives were prepared from easily accessible starting materials. The newly synthesized compounds were evaluated for their antibacterial and antifungal activities in vitro against four bacteria and two fungi.

Certain compounds containing thiazole and imidazole moieties synthesized and screen for the antimicrobial properties by Sreedevi[15]. The novel compounds synthesized were characterized by elemental analysis, IR and ^{1}HNMR spectral data. The antimicrobial activity of novel compounds was evaluated by cup plate method. A few of the synthesized compounds showed more antibacterial activity than that of the standard.



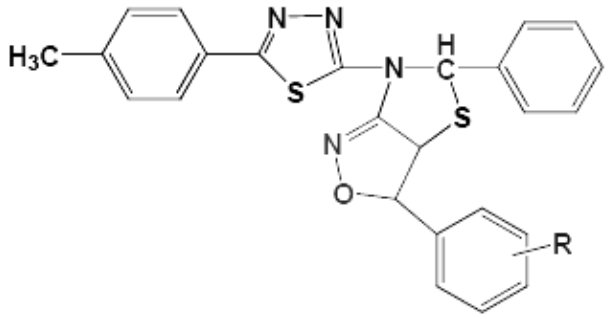
[5]

Thiazole nucleus has been established as the potential entity in the largely growing chemical world of heterocyclic compounds possessing promising pharmacological characteristics by Mishra[16]. A series of pyrazoline thiazole derivatives were synthesized with an objective to develop novel and potent antimicrobial agents of synthetic origin. The required starting material 2-amino-4-aryl thiazole was synthesized via a multicomponent condensation between thiourea, acetophenone and bromine. The thiazole was reacted with p-chloroacetophenone and various substituted aldehydes to synthesize the intermediates which on cyclization with hydrazine hydrate yielded final products i.e. pyrazoline thiazole derivatives. Synthesized compounds were purified, characterized and evaluated for their antimicrobial activity. Most of the compounds exhibited moderate to significant activities.



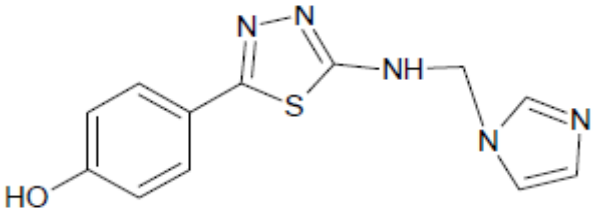
[6]

Seelam[17] synthesized a new class of 1, 3, 4-thiadiazoles which are incorporating with isoxazolo-thiazole moieties were synthesized by the reaction of chalcone derivatives of [1, 3, 4] thiadiazol-2-yl)-thiazolidin-4-one with hydroxylamine hydrochloride. The chemical structures of these compounds were confirmed by IR, NMR (1H & 13C) and mass spectral studies. The new synthesized compounds were evaluated for their antimicrobial activity. The final results revealed that some of the compounds were exhibited well antimicrobial activity compared to the standard drugs.



[7]

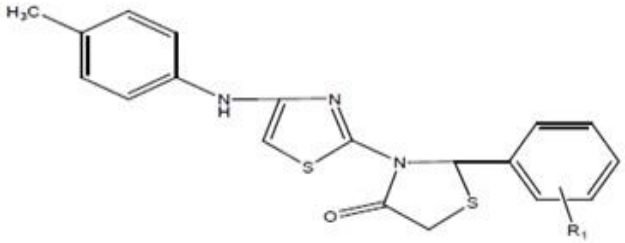
Raj[18] worked on novel thiadiazoles from 4-hydroxybenzoic acid and thiosemicarbazide. From these compounds various derivatives of 1,3,4-Thiadiazole derivatives have been synthesized. The chemical structures of the synthesized compounds were confirmed by means of IR, 1H NMR, and nitrogen estimation. These compounds were screened for antibacterial (*Staphylococcus aureus* ATCC 9144, *Bacillus Cereus* ATCC 11778, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 2853 and anti-fungal (*Aspergillus niger* ATCC 9029 and *Aspergillus fumigatus* ATCC 46645) by paper disc diffusion technique.



[8]

A review by Jain[19] reviewed on antibiotics was evident enough to establish that thiazoles are potent antimicrobial and antioxidant compounds. From the review it was also evident that the thiazole nucleus possesses the potential to be lead molecules for antimicrobial action.

Series of new 3-(4-(p-toluidino) thiazol-2-yl)-2-phenylthiazolidin-4-one derivatives were synthesized by kumar[20] from novel schiff base of 2-((4-(p-toluidino) thiazol-2-ylimino)methyl)phenol with thioglycolic acid in presence of anhydrous zinc chloride. The chemical structures of these compounds were confirmed by various physic-chemical methods viz, IR, 1H NMR, mass spectral data and elemental analysis. Newly synthesized compounds were screened in vitro for their antimicrobial activity against varieties of gram +ve and gram -ve bacterial strains such as *Bacillus subtilis*, *Pseudomonas aeruginosa* and fungi strain *Candida albicans* & *Aspergillus niger* at 40 µg/mL. The chloro and bromo substituted 2,3-substituted thiazolidin-4-one derivatives are showing activity as compare to the other functional groups.



[9]

Kumar[21] reviewed on newer antimicrobial compounds and found that antimicrobial research still remains an area of intensive investigation in the field of medicinal chemistry due to resistance developed by micro-organism to conventional antibiotics. Hydrazide-hydrazone derivatives play an important role in development of various pharmacological activities such as anticonvulsant, antimalarial, analgesic, anti-inflammatory, antiplatelet, antimicrobial, antihypertensive, antiviral, anti-tubercular, antiproliferative and antitumor activities. This review highlights antimicrobial activity shown by various hydrazide-hydrazone derivatives.

Mishra[22] reviewed on cinnoline derivatives and found that cinnolines to elicit many pharmacological actions like anti-hypertensive, antithrombotic, antihistamine, antileukemic, CNS activity, anti-tumor, antibacterial and antisecretory activity. Imidazole can be found in many other drugs such as dacarbazine, metronidazole, cimetidine, flumazenil, thyroliberin, methimazole, pilocarpine and etomidate which are used as antineoplastic antibiotic, antiulcerative, benzodiazepine antagonist, prohormone, antihyperthyroid, muscarinic receptor. In the substituted Cinnoline Imidazole series, the compounds which conatin halogen primarily chloro Substituted were showed potent antibacterial, anti-inflammatory and anti-fungal activity than other compounds. However methyl substituted compound also showed more potent antimicrobial activity and anti-inflammatory activity.

New series of 4-methyl-2-(pyridin-4-yl)-thiazole-5-yl-azoles were synthesized starting from 4-methyl-2-(pyridin-4-yl)-thiazole-5-carbohydrazide by Oniga[23]. The newly synthesized compounds were characterized by analytical 1H NMR, 13C NMR and mass spectral data. The synthesized compounds were screened for their antimicrobial activities against several strains of Grampositive and Gram-negative bacteria and one fungal strain (*Candida albicans*).

Babu[24] reviewed on quinazolinones and found them as an important chemical, synthesis of various physiological significance and pharmacological utility. Quinazolines are a large class of active chemical compounds exhibiting a broad spectrum of biological activities in animals as well as in humans.

Saravanan[25] synthesized novel thiazoles by incorporation of pyrazole moiety at 2nd position of 2-hydrazinyl-N-(4-phenylthiazol-2-yl) acetamide (5) by treating with chalcones. The chemical structures of the synthesized compounds were confirmed by means of IR, 1H-NMR, Mass spectral and Elemental analysis. These compounds were screened for anti-bacterial (*Staphylococcus aureus* ATCC 9144, *Staphylococcus epidermidis* ATCC 155, *Micrococcus luteus* ATCC 4698, *Bacillus cereus* ATCC 11778, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 2853, and *Klebsiella pneumoniae* ATCC 11298)) and anti-fungal (*Aspergillus niger* ATCC 9029 and *Aspergillus fumigatus* ATCC 46645) activities by paper disc diffusion technique. Most of the synthesized compounds exhibited significant anti-bacterial and anti-fungal activities. Among the synthesized compounds, 2-(5-(4-hydroxyphenyl)-3-phenyl-4,5-dihydro-pyrazol-1-yl)-N-(4- phenylthiazol-2-yl)acetamide was found to exhibit the highest anti-bacterial activity and 2-(5-(4-hydroxy-3-methoxyphenyl)-3-phenyl-4,5-dihydro-pyrazol-1-yl)-N-(4-phenylthiazol-2-yl)acetamide exhibited highest anti-fungal activity.

Alam[26] worked on series of novel 1, 3, 5- trisubstituted pyrazole derivatives synthesized by the reaction of substituted chalcones with hydrazine hydrate. The starting material, chalcones were prepared by Claisen Schmidt condensation of acetophenone with aldehydes in the presence of sodium hydroxide in ethanol. All the synthesized compounds were characterized by IR, 1H-NMR, and Elemental Analysis.

Prasad[27] dealt with condensation of urea, thiourea, semicarbazide and thiosemicarbazide with Ethyl-4[(chloroacetyl) amino] benzoate under microwave irradiation in the presence of ethanol to afford two oxazole and thiazole derivatives. The synthesized compounds were characterized by spectral data such as IR, NMR; Mass. Compounds were screened for antimicrobial activity against strains of gram positive, and gram negative and fungal strains. All compounds showed good antibacterial and antifungal activity.

New Triazole derivative was synthesized by cyclization reactions by Abdul Rasool[28]. Cyclization of the intermediate by the reaction of hydrazine hydrate with carbon disulfide was done to obtain the compounds. The result showed that the compounds possess high biological activity.

Reddy[29] synthesized and characterized 3-(7-Chloro-6-fluoro benzo [d] thiazol-2-yl)-2-(4-Chlorophenyl) thiazol 1,3 lidin-4-one by the reaction of substituted -2-aminobenzothiazole with aromatic amines (para amino benzoicacid, diphenylamine, morpholine, dimethylamine and diethylamine) followed by condensation with mercaptoacetic acid. All the synthesized compounds were characterized by elemental analysis, IR Spectra, 1H NMR and Mass Spectral studies. These were screened for anthelmintic activity.

Reddy[30] synthesized, characterized and evaluated the antimicrobial activity of certain novel 3-methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro-pyrazol-1-yl]-acetic acid N|-(4-substituted thiazol-2-yl)-hydrazides.

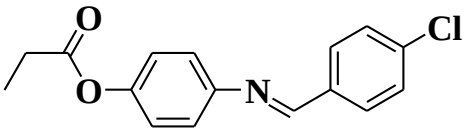
Gangwar[31] synthesized thiozolidinones derivatives from 1-actynaphthalene. 1-actynaphthalene on brominating with chloroform gives 1-bromoactynaphthalene which was reacted with substituted benzaldehyde thiosemicarbazone in ethanol as a solvent give 4-naphthalen-1-yl-2-{2-[(substituted phenyl) methylidene] hydrazino}-1,3-thiazole. This compound on addition reaction with thioglycolic acid in presence of zinc chloride as a catalyst and dioxane as a solvent gives the final compounds. Their structure has been well characterized by physical and spectral data. The new molecules have been evaluated for their potential anti-inflammatory and analgesic activity.

Moorthy[32] synthesized two series of 2, 4 thiazolidinedione derivatives containing substituted imidazoles and one series of 5-substituted 2, 4-thiazolidinedione derivatives. The chemical structures of all the three series of 2,4 thiazolidinedione derivatives have been elucidated by spectral studies (IR, 1H NMR, 13C NMR and Mass spectra). The compounds were screened for their anti-bacterial activity against *Staphylococcus aureus* ATCC-9144, *Staphylococcus epidermidis* ATCC-155, *Escherichia coli* ATCC-25922, *Pseudomonas aeruginosa* ATCC-2853 bacterial species and antifungal activity against *Aspergillus niger* ATCC- 9029, *Aspergillus fumigatus* ATCC-46645 by the paper disc diffusion technique. All other compounds had shown mild to moderate antibacterial and antifungal activities.

Idhayadhulla[33] described pyrrole derivatives with potent antibacterial and antifungal activity. A new series of pyrrole derivatives were synthesized using standard amination reactions. All the compounds were obtained with high yields and under easy experimental conditions. Synthesized compounds were characterized by IR, 1H NMR, 13C NMR, mass spectra and mass spectral fragmentation. Synthesized

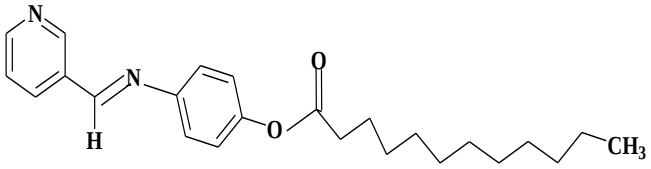
compounds were screened against *E. coli* and *S. aureus* for antibacterial activity, as well as against *A. niger* and *C. albicans* for antifungal activity. The compounds were having either with higher or equal potency to the reference compounds (Ciprofloxacin and Clotrimazole).

Sie Tiong Ha[34] reported new mesogenic Schiff base esters with polar chloro substituent.



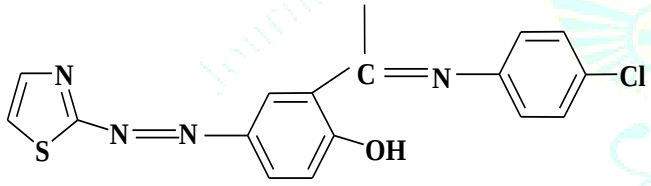
[10]

Sie-Tiong Ha[35] reported synthesis of new Schiff base 4-[(pyridine 3-ylmethylene)-amino] phenyldodecanoate.



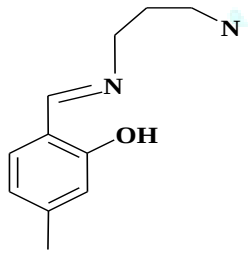
[11]

L V Gavali[36] reported synthesis and characterization of the complexes of some transition metal with 4-[2-hydroxy salicylidene-5(2-thiazolyazo] chlorobenzene.



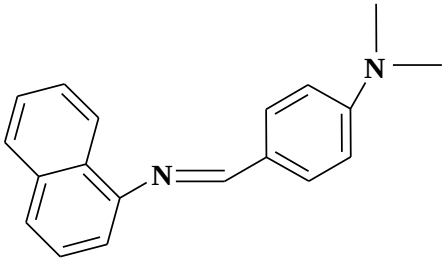
[12]

Hassan keypour[37] reported synthesis of two potentially heptadentate Schiff base ligands derived from condensation of tres (3-aminopropyl)-amine and salicylaldehyde and Nickel(II) and Copper(II) Complexes of the Former Ligand



[13]

Mohamed N. Ibrahim[38] reported synthesis, characterization and use of Schiff bases as fluorimetric analytical reagent.



[14]

CONCLUSION

Thiazole derivatives have been reported to possess broad spectrum of pharmacological activities like antidiabetic[39], CNS depressant[40], analgesic[41], antifilarial[42], antifungal and antibacterial[43], anthelmintic and antitumoral[44] activities. Mostly thiazole derivatives are known to possess intresting biological properties that show anticancer and antimicrobial activities.

This has been noticed that modifications on thiazole moiety displayed valuable biological activities, and in future more. Investigation must be carried out to evaluate more activities of thiazole against various diseases.

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